

## Remarks

### Priority

The priority information has been updated as requested. Applicants will obtain and provide a certified copy of the PCT/US00/05409 application.

### Information Disclosure Statement

Applicants will resubmit the IDS with copies of the references missing from the parent application files.

### ATCC Deposit Receipt

A copy of the receipt for ATCC Patent Deposit PTA-1640 accompanies this amendment.

### Rejection of Claims 40-60 Under 35 U.S.C. § 112

Claims 40-60 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. Claims 59 and 60 are canceled. Applicant respectfully traverses the rejection of claims 40-58.

The Office Action identifies several recitations which it asserts the specification does not support. The support for each of these is indicated in the following table.

Claims	Recitation	Support
40, 47, 54	“contacting a sample comprising a polypeptide....”	page 52, lines 8-11: “...an assay of the present invention is a cell-free assay in which a TWIK protein or biologically active portion thereof is

		contacted with a test compound and the ability of the test compound to bind to the TWIK protein or biologically active portion thereof is determined.”
54	“a polypeptide comprising a fragment of at least 15 contiguous amino acids.”	page 7, lines 7-10: “...wherein the fragment comprises at least 15 amino acids (e.g., contiguous amino acids) of the amino acid sequence of SEQ ID NO: 2, SEQ ID NO:5, SEQ ID NO:8, SEQ.ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number PTA-1640.”
41, 48, 55	“wherein the polypeptide further comprises heterologous sequences.”	page 7, lines 23-25: The proteins of the present invention or biologically active portions thereof, can be operatively linked to a non-TWIK polypeptide (e.g., heterologous amino acid sequences) to form fusion proteins.
45, 52	“an activity of the polypeptide”	page 7, lines 35-38: In another aspect, the present invention provides a method for detecting the presence of TWIK activity in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of TWIK activity such that the presence of TWIK activity is detected in the biological sample.
46, 53	“an assay for measuring release of neurotransmitters”	page 51, lines 8-9: “...by monitoring, for example, the release of a neurotransmitter from a cell which expresses TWIK.”
46, 53	“an assay for measuring membrane excitability”	page 23, lines 28-31: “In a preferred embodiment, a mutant TWIK protein can be assayed for the ability to ...(4) modulate membrane excitability....”

46, 53	“an assay for measuring cellular signaling”	page 52, lines 1-3: “For example, the activity of the target molecule can be determine by detecting induction of a cellular second messenger of the target . . . .”
44, 51, 58	“immunoassay”	page 36, lines 27-29: “Moreover, an anti-TWIK antibody can be used to detect TWIK protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the TWIK protein.”
45	“activity of the polypeptide”	page 14, lines 14-21: The biological activities of TWIK are described herein. For example, the TWIK proteins of the present invention can have one or more of the following activities: (1) modulate the release of neurotransmitters, (2) modulate membrane excitability, (3) influence the resting potential of membranes, (4) modulate wave forms and frequencies of action potentials, (5) modulate thresholds of excitation, and (6) modulate processes which underlie learning and memory, such as integration of sub-threshold synaptic responses and the conductance of back-propagating action potentials.

The specification fully supports claims 40-58. Please withdraw the rejection.

Respectfully submitted,  
BANNER & WITCOFF, LTD.

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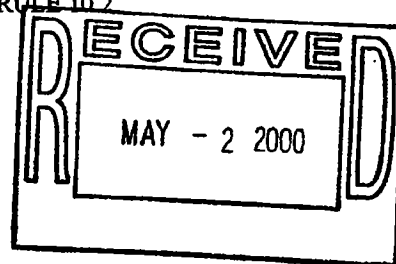
## BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

### INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3  
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Millennium Pharmaceuticals, Inc.  
Attn: Gail Mays  
75 Sidney Street  
Cambridge, MA 02139



Deposited on Behalf of: Millennium Pharmaceuticals, Inc.

**Identification Reference by Depositor:**

*Escherichia coli* with plasmid EpfbhX23553  
*Escherichia coli* with plasmid EpfbhX51164  
*Escherichia coli* with plasmid EpfbhX23222  
*Escherichia coli* with plasmid EpfbhX17867  
*Escherichia coli* with plasmid EpfbhX22012  
*Escherichia coli* with plasmid EpfbhX22025

**Patent Deposit Designation**

PTA-1639  
PTA-1640  
PTA-1641  
PTA-1642  
PTA-1643  
PTA-1644

The deposits were accompanied by:    a scientific description    a proposed taxonomic description indicated above. The deposits were received April 5, 2000 by this International Depository Authority and have been accepted.

AT YOUR REQUEST:   X   We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested April 12, 2000. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

  
Barbara E. Coupé, Administrator, Patent Depository

Date: April 27, 2000

cc: Ted Allen